WEST Search History

DATE: Thursday, July 11, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L8	L6 and @ad< 19971029	13	L8
L7	L6 and @ad< 199710029	35	L7
L6	(mhc near (class adj II)) same((single adj chain) or sc)	35	L6
L5	5869270	9	L5
DB=USPT; PLUR=YES; OP=OR			
L4	5869270	6	L4
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L3	L2 and ((single adj chain) or sc)	19	L3
L2	L1 and (mhc near (class adj II))	26	L2
L1	(rhode)[in] or (avecedo)[in] or (burkhart)[in] or (jiao)[in] or (wong)[in]	17066	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 09:46:15 ON 11 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:46:26 ON 11 JUL 2002

L1	5066	S RHODE P?/U OR ACEVEDO J?/AU OR BURKHARDT M?/AU OR JIAO J?/AU
L2	16	S L1 AND MHC
L3	12	DUP REM L2 (4 DUPLICATES REMOVED)
L4	48960	S MHC AND (CLASS (1N) II)
L5	6940	S L4 (P) ((SINGLE (1N) CHAIN) OR SC?)
L6	47202	S MHC (P) (CLASS (1N) II)
L7	3851	S L6 (P) ((SINGLE (1N) CHAIN) OR SC?)
L8	167	S L7 (P) (MULTIMER? OR POLYMER? OR JOIN? OR TETRAMER?)
L9	70	DUP REM L8 (97 DUPLICATES REMOVED)
L10	8	S L9 AND PD<1997102

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NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
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NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded
NEWS 22	Jul 02	FOREGE no longer contains STANDARDS file segment

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FILE 'HOME' ENTERED AT 09:46:15 ON 11 JUL 2002

=> file medline caplus embase biosis
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FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 09:46:26 ON 11 JUL 2002

FILE 'CAPLUS' ENTERED AT 09:46:26 ON 11 JUL 2002
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FILE 'BIOSIS' ENTERED AT 09:46:26 ON 11 JUL 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s Rhode P?/u or acevedo J?/au or burkhardt M?/au or jiao J?/au or wong H?/au
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
L1 5066 RHODE P?/U OR ACEVEDO J?/AU OR BURKHARDT M?/AU OR JIAO J?/AU OR WONG H?/AU

=> s l1 and mhc
L2 16 L1 AND MHC

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

=> dis l3 1-12 ibib abs

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:868803 CAPLUS
DOCUMENT NUMBER: 135:370658
TITLE: Modulation of T-cell receptor interactions
INVENTOR(S): Rhode, Peter; Wittman, Vaughan; Weidanz, Jon A.; **Burkhardt, Martin**; Card, Kimberlyn F.; Tal, Rony; **Acevedo, Jorge**; **Wong, Hing C.**
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090747	A2	20011129	WO 2001-US15699	20010516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-206920P P 20000525

AB Disclosed are methods for identifying compds. that modulate the interaction between T cell receptors (TCR) and major histocompatibility complex (**MHC**) antigens. The invention has many useful applications including providing high throughput screening assays for detecting compns. that can modulate an immune response.

L3 ANSWER 2 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:6971 BIOSIS
DOCUMENT NUMBER: PREV200200006971
TITLE: **MHC** molecules and uses thereof.
AUTHOR(S): Rhode, Peter R.; **Jiao, Jin-An (1)**; **Burkhardt, Martin; Wong, Hing C.**
CORPORATE SOURCE: (1) Fort Lauderdale, FL USA
ASSIGNEE: Sunol Molecular Corporation
PATENT INFORMATION: US 6309645 October 30, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 30, 2001) Vol. 1251, No. 5, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB The present invention relates to novel complexes of major histocomability complex (**MHC**) molecules and uses of such complexes. In one aspect, the invention relates to loaded **MHC** complexes that include at least one **MHC** molecule with a peptide-binding groove and a presenting peptide non-covalently linked to the **MHC** protein. In another aspect, the invention features single chain **MHC** class II peptide fusion complexes with a presenting peptide covalently linked to the peptide binding grove of the complex. **MHC** complexes of the invention are useful for a variety of applications including: 1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and 2) methods for suppressing or inducing an immune response in a mammal.

L3 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:499745 BIOSIS
DOCUMENT NUMBER: PREV200100499745
TITLE: Soluble **MHC** complexes and methods of use thereof.
AUTHOR(S): Rhode, Peter R.; **Acevedo, Jorge (1)**; **Burkhardt, Martin; Jiao, Jin-an; Wong, Hing C.**
CORPORATE SOURCE: (1) Miami, FL USA
ASSIGNEE: Sunol Molecular Corporation
PATENT INFORMATION: US 6232445 May 15, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 15, 2001) Vol. 1246, No. 3, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB The present invention relates to novel complexes of major histocompability complex (**MHC**) molecules and uses of such complexes. In one aspect, the invention relates to single chain **MHC** class II complexes that include a class II beta2 chain modification, e.g., deletion of essentially the entire class II beta2 chain. In another aspect, the invention features single chain **MHC** class II which comprise an immunoglobin constant chain or fragment. Further provided are polyspecific **MHC** complexes comprising at least one single chain **MHC** class II molecule. **MHC** complexes of the invention are useful for a variety of applications including: 1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and 2) methods for suppressing or inducing an immune response in a mammal.

L3 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:277860 CAPLUS
DOCUMENT NUMBER: 132:320940
TITLE: Polyspecific binding molecules and uses thereof
INVENTOR(S): Weidanz, Jon A.; Card, Kimberlyn; Sherman, Linda A.; Klinman, Norman R.; **Wong, Hing C.**
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023087	A1	20000427	WO 1999-US24645	19991021

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1124568	A1	20010822	EP 1999-970601	19991021

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-105164P P 19981021
WO 1999-US24645 W 19991021

AB The present invention relates to polyspecific binding mols. and

particularly single-chain polyspecific b[illegible]ng mols. that include at least one single-chain T-cell receptor (s.c.-TCR) covalently linked through a peptide linker sequence to at least one single-chain antibody (s.c.-Ab). The polyspecific binding mols. activate immune cells (e.g. cytotoxic T cells, NK cells or macrophages) and kill target cells (e.g. tumor cells or virally infected cells). The polyspecific binding mols. are useful for diagnosis and treatment of cancers and viral infections.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 12 MEDLINE
ACCESSION NUMBER: 2000442218 MEDLINE
DOCUMENT NUMBER: 20443576 PubMed ID: 10990169
TITLE: Immune cell signaling in lupus.
AUTHOR: Tsokos G C; **Wong H K**; Enyedy E J; Nambiar M P
CORPORATE SOURCE: Department of Medicine, Uniformed Services University of the Health Sciences, and Walter Reed Army Institute of Research, Silver Spring, Maryland 20910-7500, USA..
gtsokos@usa.net
CONTRACT NUMBER: AI 422269 (NIAID)
SOURCE: CURRENT OPINION IN RHEUMATOLOGY, (2000 Sep) 12 (5) 355-63.
Ref: 60
Journal code: 9000851. ISSN: 1040-8711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104
AB The fate of the lymphocyte is determined by integration of signals delivered after the binding of antigen to the surface antigen receptor, signals delivered by cytokines that bind to their surface receptors, and signals initiated after the engagement of other surface receptors, known as costimulatory molecules. The summation of this input determines whether the immune cell will become stimulated, ignore the signal (anergy), or die (apoptosis). Antigen-receptor signaling events are abnormal in lupus lymphocytes, manifested by increased calcium responses and hyperphosphorylation of several cytosolic protein substrates. Further down, at the gene transcription level, the activity of the nuclear factor kappaB is decreased. These events are underwritten by defective T cell receptor zeta chain expression, overexpression of the gamma chain of the Fc(epsilon)RI that functions as an alternate of zeta chain, and decreased p65 -Rel A protein that is responsible for the inducible NFkappaB activity. Accumulated research data have enabled us to begin deciphering the molecular basis of the abnormal lupus lymphocyte and may lead to the development of new medicinal treatments for lupus.

L3 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:297317 CAPLUS
DOCUMENT NUMBER: 130:295539
TITLE: Construction of chimeric soluble **MHC** complexes
INVENTOR(S): Rhode, Peter R.; **Acevedo, Jorge**; **Burkhardt, Martin**; **Jiao, Jin-an**; **Wong, Hing C.**
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921572	A1	19990506	WO 1998-US21520	19981013
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6232445	B1	20010515	US 1997-960190	19971029
CA 2307178	AA	19990506	CA 1998-2307178	19981013
AU 9898001	A1	19990517	AU 1998-98001	19981013
EP 1027066	A1	20000816	EP 1998-952256	19981013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508300	T2	20020319	JP 2000-517730	19981013

PRIORITY APPLN. INFO.: US 1997-960190 A 19971029
WO 1998-US21520 W 19981013
AB The authors disclose the construction and expression of sol. single-chain (s.c.) **MHC** class II mols. In one aspect, the s.c.-**MHC** class II mols. include a .beta.2 chain modification, e.g., deletion of essentially the entire class II .beta.2 domain. In another aspect, the invention features single-chain **MHC** class II which contain an Ig light chain const. region fragment (CL). The CL fragment allows multimerization of single-chain monomers of identical or disparate **MHC** specificity or formation of heteromeric mols. with effector function (e.g., single-chain antibodies). In addn., the sol. **MHC** class II mols. can be constructed for exogenous loading of cognate peptides or the requisite peptides can be included in the single-chain constructs themselves. In one example, single-chain I-Ad mols. were constructed as fusion proteins with T-cell epitopes from either ovalbumin or glycoprotein D of herpes simplex virus. These constructs were shown to stimulate interleukin-2 prodn. by their resp. antigen-specific T-cells. **MHC** complexes of the invention are useful for a variety of applications including: (1) in vitro screens for identification and isolation of peptides that modulate activity of selected T-cells, including peptides that are T cell receptor antagonists and partial agonists, and (2) methods for suppressing or inducing an immune response in a mammal.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:246173 BIOSIS

DOCUMENT NUMBER: PREV199900246173
TITLE: Single chain MHC complexes and uses thereof.
AUTHOR(S): Rhode, P. R.; Jiao, J-A.; Burkhardt, M. ; Wong, H. C.
CORPORATE SOURCE: Miami, Fla. USA
ASSIGNEE: SUNOL MOLECULAR CORPORATION
PATENT INFORMATION: US 5869270 Feb. 9, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 9, 1999) Vol. 1219, No. 2, pp. 1524. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L3 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:618856 CAPLUS
DOCUMENT NUMBER: 129:229693
TITLE: Fusion proteins comprising bacteriophage coat protein and a single-chain T cell receptor
INVENTOR(S): Weidanz, Jon A.; Card, Kimberlyn F.; Wong, Hing C.
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839482	A1	19980911	WO 1998-US4274	19980305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9866856	A1	19980922	AU 1998-66856	19980305
EP 977886	A1	20000209	EP 1998-908950	19980305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001514503	T2	20010911	JP 1998-537984	19980305

PRIORITY APPLN. INFO.: US 1997-813781 A 19970307
WO 1998-US4274 W 19980305

AB The present invention relates to novel fusion proteins comprising a bacteriophage coat protein and a single-chain T cell receptor and uses of such complexes. In one aspect, the invention relates to sol. fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor which comprises a V-.alpha. gene covalently linked to a V-.beta. chain by a peptide linker sequence. The single-chain TCR fusion protein typically also includes one or more fused protein tags to help purify the fusion protein from cell components which can accompany it. The TCR used was murine DO11.10 cell TCR which recognizes and binds a chicken ovalbumin peptide spanning amino acids 323-339 in the context of an I-Ad MHC class II mol. The sol. fusion proteins of the invention are useful for a variety of applications including: (1) making a bacteriophage library for displaying single-chain T cell receptors for use in screens for identification and isolation of ligands that bind single-chain T cell receptors, and (2) methods for isolating sol. and fully functional single-chain T cell receptors from the fusion proteins. The single-chain TCR fusion proteins can be made without performing difficult solubilization, protein refolding or cleaving steps; formation of inclusion bodies in expressing cells is minimal, thereby significantly increasing yields.

L3 ANSWER 9 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999110189 MEDLINE
DOCUMENT NUMBER: 99110189 PubMed ID: 9894898
TITLE: Display of functional alphabeta single-chain T-cell receptor molecules on the surface of bacteriophage.
AUTHOR: Weidanz J A; Card K F; Edwards A; Perlstein E; Wong H C
CORPORATE SOURCE: Sunol Molecular, Miramar, FL 33025, USA.. jaweid@laker.net
CONTRACT NUMBER: R43-CA76856-01 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1998 Dec 1) 221 (1-2) 59-76.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990129

AB The ability to display functional T-cell receptors (TCR) on the surface of bacteriophage could have numerous applications. For instance, TCR phage-display could be used to develop new strategies for isolating TCRs with unique specificity or it could be used to carry out mutagenesis studies on TCR molecules for analyzing their structure-function. We initially selected a TCR from the murine T-cell hybridoma, DO11.10, as our model system, and genetically engineered a three domain single-chain TCR (scTCR) linked to the gene p8 protein of the Escherichia coli bacteriophage fd. Immunoblotting studies revealed that (1) E. coli produced a soluble scTCR/p8 fusion protein and (2) the fusion protein was packaged by the phage. Cellular competition assays were performed to evaluate the functionality of the TCR and showed the DO11.10 TCR-bearing phage could significantly inhibit stimulation of DO11.10 T hybridoma cells by competing for binding to immobilized MHC/peptide IA(d)/OVA(323-339). Flow cytometric analysis was carried out to evaluate direct binding of DO11.10 TCR-bearing phage onto the surface of cells displaying either IAd containing irrelevant peptide or OVA peptide. The results revealed binding of DO11.10 TCR-bearing phage only on cells expressing IA(d) loaded with OVA peptide showing TCR fine specificity for peptide. To illustrate the generality of TCR phage-display, we also cloned and displayed on phage a second TCR which recognizes a peptide fragment from human tumor suppressor protein p53 restricted by HLA-A2. These findings demonstrate functional TCR can be displayed on bacteriophage potentially leading to the development of novel applications involving TCR phage-display.

L3 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002
ACCESSION NUMBER: 1997:533677 CAPLUS
DOCUMENT NUMBER: 127:204455
TITLE: Preparation and immunomodulatory activity of single-chain **MHC** mols.
INVENTOR(S): Rhode, Peter R.; **Jiao, Jin-An**; **Burkhardt, Martin**; **Wong, Hing C.**
PATENT ASSIGNEE(S): Dade International, Inc., USA; Rhode, Peter R.; Jiao, Jin-An; Burkhardt, Martin; Wong, Hing C.
SOURCE: PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9728191	A1	19970807	WO 1997-US1617	19970130
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5869270	A	19990209	US 1996-596387	19960131
CA 2244755	AA	19970807	CA 1997-2244755	19970130
AU 9722538	A1	19970822	AU 1997-22538	19970130
AU 729672	B2	20010208		
EP 877760	A1	19981118	EP 1997-905709	19970130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, PI				
JP 2000515363	T2	20001121	JP 1997-527863	19970130
US 6309645	B1	20011030	US 1998-67615	19980428
US 2002034513	A1	20020321	US 2001-848164	20010503

PRIORITY APPLN. INFO.: US 1996-596387 A 19960131
WO 1997-US1617 W 19970130
US 1998-67615 XX 19980428

AB The present invention relates to novel complexes of major histocompatibility complex (**MHC**) mols. and uses of such complexes. In one aspect, the invention relates to loaded **MHC** complexes that include at least one **MHC** mol. with a peptide-binding groove and a presenting peptide non-covalently linked to the **MHC** protein. In another aspect, the invention features single chain **MHC** class II peptide fusion complexes with a presenting peptide covalently linked to the peptide binding groove of the complex. **MHC** complexes are useful for a variety of applications including: (1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and (2) methods for suppressing or inducing an immune response in a mammal.

L3 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:302467 CAPLUS
DOCUMENT NUMBER: 124:340931
TITLE: Histocompatibility antigen **MHC** fusion products with T-cell receptor antagonist or other presenting peptide, recombinant fusion protein, and use for immune response regulation and T-cell-modulator screening
INVENTOR(S): **Wong, Hing C.**; Rhode, Peter R.; Weidanz, Jon A.; Grammer, Susan; Edwards, Ann C.; Chavaillaz, Pierre-Andre; **Jiao, Jin-An**
PATENT ASSIGNEE(S): Dade International, Inc., USA
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9604314	A1	19960215	WO 1995-US9816	19950731
W: AU, CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2196085	AA	19960215	CA 1995-2196085	19950731
AU 9534039	A1	19960304	AU 1995-34039	19950731
AU 696177	B2	19980903		
EP 776339	A1	19970604	EP 1995-930790	19950731
EP 776339	B1	20001011		
R: BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL				
JP 10503379	T2	19980331	JP 1995-506744	19950731
EP 997477	A2	20000503	EP 1999-124343	19950731
EP 997477	A3	20020710		
R: BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL				
ES 2152424	T3	20010201	ES 1995-930790	19950731

PRIORITY APPLN. INFO.: US 1994-283302 A2 19940729
US 1995-382454 A 19950201
EP 1995-930790 A3 19950731
WO 1995-US9816 W 19950731

AB The present invention relates to novel complexes of major histocompatibility complex (**MHC**) mols. and uses of such complexes. In particular, the invention relates to **MHC** fusion complexes that contain an **MHC** mol. with a peptide-binding groove and a presenting peptide covalently linked to the **MHC** protein. Fusion complexes of the invention are useful for a variety of applications including in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, methods of suppressing an immune response of a mammal and methods for inducing an immune response in a mammal.

L3 ANSWER 12 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97098715 MEDLINE
DOCUMENT NUMBER: 97098715 PubMed ID: 8943392
TITLE: Single-chain **MHC** class II molecules induce T cell activation and apoptosis.
AUTHOR: Rhode P R; **Burkhardt M**; **Jiao J**; Siddiqui A H; Huang G P; **Wong H C**
CORPORATE SOURCE: Sunol Molecular Corporation, Miami, FL 33172, USA.

SOURCE: JOURNAL OF IMMUNOLOGY, (19[redacted]c 1) 157 (11) 4885-91.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961227

AB **MHC** class II/peptide complexes displayed on the surface of APCs play a pivotal role in initiating specific T cell responses. Evidence is presented here that components of this heterotrimeric complex can be genetically linked into a single polypeptide chain. Soluble single-chain (sc) murine class II IA(d) molecules with and without covalently attached peptides were produced in a recombinant baculovirus-insect cell expression system. Correct conformation of these molecules was verified based on 1) reactivity to Abs directed against conformational epitopes in IA(d) and 2) peptide-specific recognition of the IA(d)/peptide complexes by T cells. Both sc class II molecules loaded the appropriate peptides and sc class II/peptide fusions were effective in stimulating T cell responses, including cytokine release and apoptosis. Mammalian cells were also found to be capable of expressing functional sc class II molecules on their cell surfaces. The findings reported here open up the possibility of producing large amounts of stable sc class II/peptide fusion molecules for structural characterization and immunotherapeutic applications.

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(FILE 'HOME' ENTERED AT 09:46:15 ON 11 JUL 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:46:26 ON 11 JUL 2002
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L2 16 S L1 AND MHC
L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

=> s mhc and (class (1N) II)
L4 48960 MHC AND (CLASS (1N) II)

=> s l4 (P) ((single (1N) chain) or sc?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L12 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L13 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L14 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L15 (P) '
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L6 47202 MHC (P) (CLASS (1N) II)

=> s l6 (P) ((single (1N) chain) or sc?)
3 FILES SEARCHED...
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=> s l7 (P) (multimer? or polymer? or join? or tetramer?)
L8 167 L7 (P) (MULTIMER? OR POLYMER? OR JOIN? OR TETRAMER?)

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SUP IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 70 DUP REM L8 (97 DUPLICATES REMOVED)

=> s l9 and PD<19971029
'19971029' NOT A VALID FIELD CODE
3 FILES SEARCHED...
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L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:627348 CAPLUS
DOCUMENT NUMBER: 125:298953
TITLE: Detection of a common BoLA-DRB3 deletion by sequence-specific oligonucleotide typing
AUTHOR(S): Sitte, K.; East, I. J.; Jazwinska, E. C.
CORPORATE SOURCE: Cooperative Research Centre Vaccine Technology, Queensland Institute Medical Research, Brisbane, 4029, Australia
SOURCE: Anim. Genet. (1996), 27(4), 271-273
CODEN: ANGEE3; ISSN: 0268-9146
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bovine **MHC class II** allele BoLA-DRB3*2A has an amino acid deletion of unknown function at codon 65 in the second exon, which codes for the antigen-binding site. Sequence-specific oligonucleotides were designed based on published nucleotide sequences on BoLA-DRB3 alleles, and used to detect this deletion in 51 Hereford cattle. Probes 65+ and 65- detect the presence or absence of codon 65 resp. Oligonucleotide probes were labeled with Digoxigenin (DIG), hybridized to dot blots of BoLA-DRB3 exon 2 **polymerase** chain reaction (PCR) product, and detected by chemiluminescence. Of the 51 animals **screened**, two were homozygous and 11 were heterozygous for the deletion at codon 65. The methodol. described here provides the necessary tools to **screen** rapidly for this deletion in a large no. of animals to study its effect on antigen binding and immune response.

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:114950 CAPLUS
DOCUMENT NUMBER: 124:167148
TITLE: Identification of peripheral blood dendritic cell-specific class II-related genes by differential cDNA hybridization
AUTHOR(S): Bae, Yong-Soo; Kim, Kyoung-Joo; Langhoff, Erik
CORPORATE SOURCE: Dep. of Microbiology, Hannam Univ., Daejon, 300-791,

S. Korea
SOURCE: Mol. Cells (1995), 5(6), 569-78
CODEN: MOCEEK; ISSN: 1016-8478
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We report here two peripheral blood dendritic cell (PBDC)-specific **class II**-related antigen genes identified by differential **screening** of the PBDC-cDNA library. Dendritic cells (DC) were isolated and purified from the peripheral blood leukocytes (PBL) by employing neg. selection procedure and monoclonal antibody sorting with magnetic beads. The DC-cDNA library was constructed using a .lambda.gt11 system. The cDNA library was **screened** by two steps of differential hybridization with [32P]-labeled DC-cDNA probe, and T-and monocyte-cDNA probes. Isolated clones which were potentially specific to DC were sequenced and then searched for their sequence homol. in Genbank database. Novel or interesting genes were confirmed for their sequence homol. in Genbank database. Novel or interesting genes were confirmed for their specificity to DC by checking the relative amts. of the mRNA expressed in T-cell, B-cells, monocytes and DC by **polymerase** chain reaction (PCR) and Northern blot hybridization. Through these expts., two **MHC classes** II-related genes, DM.alpha. and DM.beta., were found to be expressed only in DC among the PBL. Biol. functions of these genes remain to be solved by producing monoclonal antibodies against these gene products.

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:616955 CAPLUS
DOCUMENT NUMBER: 119:216955
TITLE: Polymeric drugs as immunomodulatory vaccines against multiple sclerosis
AUTHOR(S): Sela, Michael
CORPORATE SOURCE: Dep. Chem. Immunol., Weizmann Inst. Sci., Rehovot, 76100, India
SOURCE: Makromol. Chem., Macromol. Symp. (1993), 70-71(34th International Symposium on Macromolecules, 1992), 147-55
CODEN: MCMSES; ISSN: 0258-0322
DOCUMENT TYPE: Journal
LANGUAGE: English
AB COP-1, a synthetic basic random amino acid copolymer, is effective in suppression of exptl. allergic encephalomyelitis is guinea pigs, rabbits, mice, rhesus monkeys and baboons, and of the exacerbating-remitting type of multiple **sclerosis** in humans. COP-1 is cross-reactive at the monoclonal antibody level with the basic protein of the myelin sheath of the brain (BP), and the suppressive effect may be related to this immunol. cross-reaction. Indeed, competition for the major histocompatibility complex (**MHC**) **class II** antigen, between BP and COP-1, may be one explanation for its beneficial effect in the disease. This **polymeric** drug, COP-1, may, therefore, be considered also an immunomodulatory vaccine, and may serve as a prototype to vaccines against autoimmune diseases.

L10 ANSWER 4 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95014826 EMBASE
DOCUMENT NUMBER: 1995014826
TITLE: [Antibody defined variants of systemic sclerosis - Clinical and immunogenetic aspects]. AUTOANTIKORPER-DEFINIERTE VARIANTEN DER SYSTEMISCHEN SKLEROSE - KLINISCHE UND IMMUNGENETISCHE ASPEKTE.
AUTHOR: Genth E.
CORPORATE SOURCE: Burtscheider Markt 24,D-52066 Aachen, Germany
SOURCE: Nieren- und Hochdruckkrankheiten, (1994) 23/12 (596-604).
ISSN: 0300-5224 CODEN: NIHOD
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Systemic **sclerosis** (**scleroderma**) or **scleroderma** overlap syndromes are clinically polymorphous disorders. The skin (**scleroderma**, **scleredema**, dermatitis, vascular lesions), the vascular system (obliterating fibrosis of the arterial intima, microvascular lesions), internal organs (lungs, esophagus and lower gastrointestinal tract, heart, kidney), the locomotor system (**joints**, tendon sheats, muscles) as well as the exocrine glands (sicca syndrome) are involved in different frequency and severity. More than 95% of patients with systemic **sclerosis** have antinuclear antibodies (ANA) in the serum, the majority (about 90%) can be attributed to one of 8 **scleroderma** related autoantibody systems. These autoantibodies are virtually exclusive to each other. Autoantibodies against DNA-topoisomerase I (**Scl**-70), centromer antigens (CenP-A, CenP-B, CenP-C), RNA-**polymerase** I, II or III, Th-(To-)RNP or fibrillarin (U3-RNP) are serological markers of systemic **sclerosis**, whereas antibodies against U1-nRNP, PM-**Scl** or Ku are more frequently found in patients with **scleroderma** and overlapping features of other systemic connective tissue disorders like lupus erythematosus or poly-/dermatomyositis. Based on data from the literature and our own results we will demonstrate, that patients with different **scleroderma**-related autoantibodies differ with respect to the type, frequency and severity of their clinical manifestations and with regard to their survival rate. Renal manifestations (renal crisis) are associated with more extensive **scleroderma** and antibodies to DNA-topoisomerase I or RNA-**polymerases**. The present data support the notion to classify systemic **sclerosis** or **scleroderma** -overlap syndromes on the basis of different autoantibodies. The strong association of different **scleroderma**-related autoantibodies with different **MHC class II** alleles suggests a key role of autoantibodies in the pathogenesis of these disorders.

L10 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:481708 BIOSIS
DOCUMENT NUMBER: PREV199799780911
TITLE: A candidate gene approach to animal quality traits.
AUTHOR(S): Palmer, B. R.; Hickford, J. G. H.; Bickerstaffe, R.
CORPORATE SOURCE: Molecular Biotechnol., Animal Veterinary Sci. Group, P.O. Box 84, Lincoln Univ. New Zealand
SOURCE: Proceedings of the New Zealand Society of Animal Production, (1997) Vol. 57, No. 0, pp. 294-296.
ISSN: 0370-2731.

DOCUMENT TYPE: Journal; Article
LANGUAGE: English
AB A variety of animal quality traits, particularly those associated with meat and wool production and disease resistance, have been the subject of sophisticated genetic analyses. Investigation of the biochemistry and physiology underlying disease or production traits has implicated particular proteins and hence genes as "candidates" for having major phenotypic effects. This makes the candidate gene approach a useful complement to animal genome mapping of markers and QTLs. We have applied the candidate gene approach for the sheep quality traits of meat tenderness and footrot resistance. A three allele system detected by **polymerase chain** reaction - **single** strand conformational polymorphism (PCR-SSCP) has been observed for the ovine calpastatin gene. Calpastatin is the specific inhibitor of the ubiquitous calcium-dependent proteases mu-calpain and m-calpain. There is very strong population genetic and protein assay data in cattle to inversely correlate postmortem calpastatin levels with meat tenderness. Assay of postmortem calpastatin levels in aging lamb confirms an important regulatory role for calpastatin in sheep meat aging. Data sets from preliminary experiments testing the association of the three allele ovine calpastatin system with meat tenderness values and other meat quality characteristics show significantly different fillet tenderness, early postmortem calpastatin and mu-calpain levels between ewes with different calpastatin genotypes. The early postmortem calpastatin levels and the longissimus dorsi pH at 24 hr post-mortem of sheep representing two different genotypes was also significantly different. The major histocompatibility (**MHC**) proteins of vertebrates have a role in presenting peptide fragments from pathogenic organisms to the systemic immune system. It is hypothesized that a component of resistance in sheep to footrot is based on an effective systemic immune response and hence controlled by **MHC** presentation. Sixteen alleles have been identified at the ovine **MHC class II** DQA2 locus and 8 at the DQA1 locus. A significant (p = 0.001) association between footrot status and DQA2 genotype was observed in a halfsib family challenged with the disease under standardized field conditions.

L10 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:454896 BIOSIS
DOCUMENT NUMBER: PREV199799754099
TITLE: A polycistronic retrovirus vector for expression of swine MHC class of II DR-alpha/beta heterodimers.
AUTHOR(S): Banerjee, Papia T. (1); Kaynor, G. Campbell; Muthukumar, Shanthini; Denaro, Maria; Shimada, Hideaki; Zhu, Shaochun; Rrosa, Margaret D.; Sachs, David H.; Leguern, Christian
CORPORATE SOURCE: (1) BioTransplant Inc., Charlestown, MA 02129 USA
SOURCE: Xenotransplantation, (1997) Vol. 4, No. 3, pp. 161-173. ISSN: 0908-665X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A recombinant polycistronic retroviral vector was generated to express **multimeric** proteins from a single transcript by using internal ribosomal entry sites which allow independent initiation of translation from internal cistrons. In addition, an enhancerless SV40 origin of replication was incorporated into the recombinant plasmids between the retroviral long terminal repeat sequences to facilitate the testing of expression of multiple proteins in a transient COS cell transfection assay. With the ultimate goal of utilizing these vector types for the induction of transplantation tolerance via retrovirus-mediated gene transfer (LeGuem et al. J Mol Med 1995:73:269 (I); Sachs Transplant **Sci** 1993:3:59 (2)) we have incorporated miniature swine **MHC class II** DRA and DRB cDNAs which encode for the SLA-DR-alpha and SLA-DR-beta polypeptide chains, respectively, into the retroviral construct. The proviral DNA integrated within the producer clone genome, was found to be stable over a 3-month period and no loss of expression of DR heterodimers was observed on the cell surface of either the retrovirus producer cells or the retrovirally transduced fibroblast cell line. High titers (gt 1 times 10-6 CFU/ml) of recombinant particles, devoid of replication competent helper viruses, were obtained. Such vectors represent the first successful attempt to express **multimeric** proteins at the cell surface of transduced cells.

L10 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:139350 BIOSIS
DOCUMENT NUMBER: PREV199799438553
TITLE: Single-strand conformation polymorphism analysis of the second exon of a MHC class II DRB gene in sheep.
AUTHOR(S): Jugo, B.; Martinez, N.; Estomba, A.; Vicario, A.
CORPORATE SOURCE: Dep. Anim. Biol. and Genetics, Fac. Sci., Univ. Basque Country, Basque Country Spain
SOURCE: Animal Genetics, (1996) Vol. 27, No. SUPPL. 2, pp. 53-54. Meeting Info.: 25th International Conference on Animal Genetics Tours, France July 21-25, 1996 ISSN: 0268-9146.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L10 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:270260 BIOSIS
DOCUMENT NUMBER: PREV199396000485
TITLE: Molecular cloning of major histocompatibility complex class I cDNAs from Atlantic salmon (Salmo salar.
AUTHOR(S): Grimholt, Unni Vvar Hordvik (1); Fosse, Viggo M.; Olsaker, Ingrid; Endresen, Curt; Lie, Oystein
CORPORATE SOURCE: (1) Dep. Animal Genetics, Norwegian College of Vet. Med., P.O. Box 8146 Dep., N-0033 Oslo 1 Norway
SOURCE: Immunogenetics, (1993) Vol. 37, No. 6, pp. 469-473. ISSN: 0093-7711.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The major histocompatibility complex (**Mhc**) has attracted much attention because of its immense polymorphism, its importance in transplantation, and its indisputable role in disease susceptibility in humans (Chen and Parham 1989; Hill et al. 1991) and in animals (Lie 1990). Previously, typical **Mhc** features reflected in allograft rejection and mixed leucocyte reactivity were the only indications that an **Mhc** also existed in teleost fish (Stet and Egberts 1991). The use of **polymerase** chain reaction (PCR) with degenerate oligonucleotides from conserved **Mhc** regions provided the first direct evidence for **Mhc** class I and **class II** genes in a fish, the teleost carp (Hashimoto et al. 1990). The primary aim of our study was to isolate and characterize expressed **Mhc** molecules in Atlantic salmon, and thereby provide data for further studies on evolutionary and disease aspects of the **Mhc** and its

polymorphism. An atlantic salmon-specific probe from leucocyte RNA was generated by PCR based on primers from conserved regions of known **Mhc** genes. The oligonucleotides and detailed strategies are described in an accompanying paper by Hordvik and co-workers (this issue). This salmon-specific probe was employed to **screen** a leucocyte lambda-gt10 cDNA library based on a few individuals, from which **Mhc**-positive cDNAs were derived. The cDNAs analyzed in this report were established as subclones in pGEM-7z(+)-R (Promega, Madison, WI) and sequencing was performed on double-stranded DNA with SP6, T7, and internal primers, using the procedure supplied by Multi-Pol-TM DNA sequencing Kit-R (Clontech, Palo Aita, CA). Sequence alignments and analyses were performed using the UWGCG software (Devereux et al. 1984). The FASTA program (Pearson and Lipman 1988) was used to search the EMBL database. In accordance with the nomenclature proposed by Klein and co-workers (1990), we adopted the designation **Mhc**-Sasa, as proposed by Stet and Egberts (1991), for the two partial Atlantic salmon (Salmo salar) **Mhc** nucleotide sequences which we aligned to the EMBL database. One of these clones, p18, shared sequence similarity to **Mhc class II** molecules (Hordvik et al., this issue). The other clone, p23 (1.8 kilobase (kb)), showed sequence similarity to **Mhc** class I sequences with a non-translated tail of 1200 nucleotides (nt) and an open reading frame (orf) of 190 aminoacids (aa) starting in the middle of the alpha-2 domain (Fig. 1). The latter cDNA clone was used in a second **screening** of the cDNA library, which resulted in a potential full-length clone, Sasa p30 (2.8 kb), with an orf corresponding to 343 aa and a nontranslated tail of 1800 nt (Fig. 1). The domain boundaries of Sasa p30 were assigned by alignment with other **Mhc** class I molecule (Fig. 2). The aa sequence similarities between Sasa and Xenopua, and lizard, man, mouse, chicken, and carp are striking, and support the hypothesis that the isolated cDNA clones encode salmon **Mhc** class I molecules. Both and cysteines forming intrachain disulphide bonds within the alpha-2 and alpha-3 domains, and the potential glycosylation site at N-84 (numbering is based on the salmon sequence), are conserved. In the putative Sasa p30 transmembrane region there is a stretch of 21 hydrophobic residues flanked on both sides by hydrophilic segments, indicating a membrane anchored protein. Most of the residues assumed to be directly involved in the structure of the alpha-3 domain are conserved in the salmon sequence (C-198, F-203, Y-204, P-205, W-212, G-234, Y-254, C-256, and V-258; Williams et al. 1987). Nine residues pointing into the antigenic recognition site, and probably involved in recognizing constant features on processed antigens, are conserved in the alpha-1 and alpha-2 domains of humans and mice (Bjorkman et al. 1987). These residues are also conserved in the salmon sequence (L-5, Y-7, F-21, G-25, Y-57, T-140, K-143, Y-157, and Y-169). The signal peptide may be incomplete, as the cDNA clone started with a methionine residue. Both cDNA clones contained 17 repeated CA dinucleotides 110 nt after the first stop codon. This repeated sequence is polymorphic (data will be presented elsewhere), and can be used as an **Mhc**-linked marker. The two Sasa clones, p23 and p30, differed by 24 nt representing 14 aa residues (Fig. 1). Eleven of the variable aa positions resided in the alpha-2 helical domain and only three in the alpha-3 domain. Six of the aa substitutions in the Sasa alpha-2 domain corresponded to potential human T-cell receptor interacting residues (Bjorkman et al. 1987), two of which are polymorphic in humans (res. 161) and mice (res. 153). Only one substitution corresponded to a human, polymorphic, peptide-binding residue (res. 154). It is not possible to determine from our data whether the p23 and p30 cDNA clones are alleles or originate from different genes (isotypes). However, the clustering of replacement substitutions in the alpha-2 region, and the fact that the library from which the cDNA clones were selected was derived from several individuals, supports the hypothesis that the observed variation is attributable to allelism. An amino acid comparison between the salmon alpha domains and those of carp, chicken, HLA-A, H-2K, and lizard showed the significantly lowest similarity to carp (p lt 0.05). The low similarity between salmon and carp is also reflected in the phylogenetic tree (Fig. 3) based on the membrane-proximal aa sequences of **Mhc** class I (alpha-3) and **class II** (alpha-2 and beta-2) molecules. Some of its nodes, however, mustbe viewed with caution. The tree indicates that Sasa class I alpha-3 is **jointed** to the H-2K/HLA-A node, but this is a doubtful result. Similarly, the evolutionary relationship between carp, Xenopus, and shark class I sequences are uncertain, and more **Mhc** class I sequences from lower vertebrates are needed to clarify the picture. All the **class II** sequences reside on the same branch. Shark **class II** is **joined** to a human **class II** alpha sequence, and the trout and salmon **class II** peptides are very similar and branched together with carp beta-2. Hashimoto and co-workers (1990) used degenerate primers directly on genomic DNA from carp. It could therefore be suggested that the presented carp class I sequence, in contrast to the carp **class II** sequence, originates from a pseudogene and has thus acquired a considerable number of mutations. The carp class I sequence could also represent a nonclassical carp **Mhc** molecule. Both suggestions would explain why the carp class I sequence has the lowest overall alpha domain aa similarity (20%) to salmon. Further speculation on teleostean evolution must be deferred until further information is available on expressed carp **Mhc** class I sequences. A FASTA search with the p30 cDNA sequence identified 40 **Mhc** class I sequences as being most similar to the salmon sequence. These sequences included both nonclassical (mouse Q7(b), mouse Tla(c), and human HLA-G (HLA 6.0)) and classical **Mhc** class I genes. The question as to whether Atlantic salmon has both classical and nonclassical homologues, as seen in human and mouse, will be possible to answer when more Sasa loci have been identified. In conclusion, this study, together with the work done by Hordvik and co-workers (this issue), demonstrates the existence of expressed **Mhc** class I and **class II** molecules in Atlantic salmon. The clonal variation seen in these reports indicates allelic polymorphism as seen in other species, but the number of alleles and loci involved remains to be established. The teleost **class II** beta-2 peptide sequences of salmon, trout, and carp are closely related. The relationship between salmon and carp class I alpha-3 peptides is unclear. Further information on expressed carp class I sequences is needed to resolve this.

=> dis his

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L1 5066 S RHODE P?/U OR ACEVEDO J?/AU OR BURKHARDT M?/AU OR JIAO J?/AU
L2 16 S L1 AND MHC
L3 12 DUP REM L2 (4 DUPLICATES REMOVED)
L4 48960 S MHC AND (CLASS (1N) II)

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L5          6940 S L4 (P) ((SINGLE (1N) CHAIN)       ?)
L6         47202 S MHC (P) (CLASS (1N) II)
L7          3851 S L6 (P) ((SINGLE (1N) CHAIN) OR SC?)
L8           167 S L7 (P) (MULTIMER? OR POLYMER? OR JOIN? OR TETRAMER?)
L9            70 DUP REM L8 (97 DUPLICATES REMOVED)
L10            8 S L9 AND PD<19971029

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FULL ESTIMATED COST                                      95.25      95.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -5.58      -5.58

STN INTERNATIONAL LOGOFF AT 10:04:21 ON 11 JUL 2002
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